## REMARKS

### Claim Amendments

Claims 1-46 are present in the application. Claim 26 has not been amended.

Claims 12-23 are cancelled without prejudice.

Claims 1-5, 8-11, 24, 27 and 28 are amended herein to increase the consistency of claim language between claims, correct or alter claim dependency, or to provide antecedent basis. Claim 1 is amended to specify that the mammalian subject either is suspected of having or is prone to develop a renal tubular cell injury (as supported by, e.g., paragraphs 0038, 0045, and 0101). Claim 6 is amended to delete the step of providing a treatment to the mammalian subject, and to specify in new step (a) that the sample is obtained from a mammalian subject that experienced a renal tubular cell injury and that has received a treatment for the injury, and adding the step of evaluating the renal tubular cell injury status based on the level of NGAL in the post-treatment urine sample to determine the effectiveness of the treatment (as supported by paragraphs 0038 and 0043). Claim 24 is amended to specify a new step (a) that the sample is obtained from a mammalian subject that is experiencing the event. Claim 27 is amended to clarify those events experienced by the subject. Claim 28 is amended to incorporate the limitation of Claim 29, to provide that the sample is taken within 24 hours of an event that presents a risk of developing a renal tubular cell injury in the subject, and, like Claim 6, to add a step of evaluating the renal tubular cell injury of the subject based on the level of NGAL present in the urine sample (as supported by, e.g., paragraphs 0039 and 0045-0046). Claim 7, 25 and 29 are canceled in view of the claim amendments.

New Claims 30-46 are added. New Claim 30 is based on Claim 1 as filed, wherein the steps (a) - (c) of Claim 1 have been combined into a single step of detecting the presence of the biomarker NGAL (as supported by, e.g., paragraph 0045), and wherein the claim is drawn to evaluating renal tubular injury status (as supported by, e.g.: Abstract; paragraph 0038, broadly referring to "diagnosing and quantifying the initial kidney injury", "following the response to early treatment", and "predicting long term outcome"; original Claim 22, and paragraphs 0013, and 0043-0045). New Claim 31 depends from Claim 30 and includes distinct steps (i) and (ii), as supported by original Claim 1. New Claim 46 likewise is based

on (but does not depend from) Claim 1, and like amended Claim 24 and 28, eliminates the independent step of obtaining the urine sample.

New Claim 32 specifies the nature of the renal tubular cell injury (as supported by, e.g., original Claim 1 and paragraph 0040 [second sentence]).

New Claim 33 pertains to detection of NGAL in the very first urine output of the subject immediately after onset of the injury (as supported in paragraph 0039).

New Claims 34-35 pertain to the time period within which the urine sample is obtained relative to the time of the event (as supported by paragraphs 0017, 0022-0025, 0039 and 0044).

New Claims 36-38 pertain to the method where the event makes the subject develop or be prone to develop ARF (as supported by paragraph 0045), or by a specific event (as supported by paragraphs 0038 and 0042)..

New Claims 39-43 pertain to the use of the NGAL assay result (i.e., the NGAL urine level assessed) to evaluate renal tubular cell injury by contrasting the level with a predetermined urinary NGAL level (as supported by, e.g., Examples 4-6 and Figures 9-16).

New Claims 44-45 pertain to the method carried out following treatment (as supported by, e.g., original Claim 6, original Claim 24, Abstract, paragraphs 0011).

No new matter has been added by way of the claim amendments.

Applicant believes that the amendments to the claims results in additional fee claims for two additional total claims. The $100.00 additional claims fee is attached hereto.

**Supplemental Information Disclosure Statement**

The Applicants advise the Examiner that a supplemental Information Disclosure Statement was filed on Nov. 14, 2006.

**Restrictions and Election**

The Examiner requires restriction of the claims to four distinct inventions, as follows:

I. Claims 1-5 and 28-29, stated as being drawn to methods for the detection of a renal tubular cell injury, classified in class 435, subclass 7.1.

II. Claims 6-11, stated as being drawn to a method of monitoring the effectiveness of a treatment, classified in class 436, subclass 538.

III. Claims 12-23, stated as being drawn to kits, classified in class 422, subclass 61.

IV. Claims 24-27, stated as being drawn to a method of identifying the extent of a renal tubular cell injury, classified in class 435, subclass 4.

Because the Office requires election in any response, Applicants provisionally elect Group I and Claims 1-5 and 28-29 that read upon Group I, with traverse. Applicants have cancelled Claims 12-23 of Group III. Applicants will withdraw any further non-elected claims and make any further necessary claim amendments after the Restriction Requirement has been made final. Applicants now add new Claims 30-46. Consequently, Group I now includes after amendments, independent Claims 1, 30 and 46, and dependent Claims 2-5, 9-11, and 31-45. The remaining Groups include after amendments: Group II, Claim 6 and 8; and Group IV, Claims 24, 26 and 27.

**Traversal of Restriction Requirement**

A requirement for restriction is properly made only when (1) there are two or more patentably independent and distinct inventions, and (2) the inventions cannot be simultaneously examined without serious burden on the Examiner. Applicants respectfully submit that the Restriction Requirement is not proper because it would not constitute a serious burden to search and consider each of the inventions. Each of the identified groups of claimed inventions is linked by the concept that assessment of NGAL in a urine sample can be employed to evaluate the renal tubular cell injury status of a mammalian subject. It is respectfully submitted that a complete patentability search for any one of the claimed inventions would seem to properly involve a search of references primarily pertaining to the other claimed invention because the Examiner might want to consider whether a reasonable suggestion of one of the claimed inventions could also reasonably be deemed to extend to the other claimed inventions. Accordingly, applicants respectfully request that each of the identified inventions (defined by each of Groups I to IV) be examined together.

In particular, Applicants respectfully request reconsideration of the restriction with respect to Group I (as amended, including independent Claims 1, 30 and 46, and dependent Claims 2-5, 9-11 and 31-45), Group II (as amended, including independent Claim 6, and dependent claim 8), and Group IV (as amended, including independent Claim 24, and dependent claims 26 and 27). Applicants note that independent method Claims 6 and 24 each

include every limitation of Claims 1 and 46 of Group I, as well as of new Claim 30 (the broadest claim of Group I), whereby Claim 30 is a generic claim. The allegations raised in the numbered Sections of the Office Action are addressed below.

***A. Inventions of Groups I and II:***

The Office Action alleges in Section 2 that the inventions of Groups I and II are distinct because the inventions as claimed differ materially with respect to function and effect. No reasoning is presented for this allegation. In fact, however, the function of the inventions of both Groups (as well as that of Group IV) as claimed appears to be the same – namely, the detection of NGAL in urine. Likewise, the effect of the inventions of these Groups appears to be the same – i.e., each of the inventions provide an assessment of the renal tubular cell injury status of the mammalian subject.

The Office Action also alleges that the inventions do not overlap in scope because Group I is drawn to a diagnostic method of detecting renal cell injury, while Group II is drawn to a method of monitoring effectiveness of treatment for renal cell injury, such that that patient populations are mutually exclusive and are directed, respectively to a population not yet diagnosed with injury (Group I), or already diagnosed with injury (Group II).

Applicants traverse this argument that the patient populations of Group I, and II are mutually exclusive, and further add that the patient population of Group IV also appears to be not mutually exclusive. Namely, a mammalian subject under evaluation for the presence of NGAL in the urine (Claims 1, 30 and 46 of Group I) may be a subject experiencing renal tubular cell injury that is being treated (Claim 6 of Group II) or a subject who has experienced an event and is being evaluated to determine the extent of a renal tubular cell injury (Claim 24 of Group IV). In all of these cases, it is quite possible that injury is expected, but has not yet been diagnosed.

The Office Action further alleges that the inventions as claimed do not encompass overlapping subject matter. Claims 1, 30, 46, 6 and 24 would appear to literally overlap in scope, however, because both the method of monitoring the effectiveness of a treatment for renal tubular cell injury of Claim 6, and the method of identifying the extent of a renal tubular cell injury of Claim 24, incorporate the generic method of Claims 1, 30 and 46 by detecting the presence of the biomarker NGAL in the urine sample. Accordingly the claimed inventions as encompassed by Groups I, II and IV would appear to literally overlap in scope.

***B. Inventions of Groups I (II) and IV:***

The Office Action alleges in Section 3 that the inventions of Groups I (II) and IV are distinct because: (a) the invention of Group I is drawn to a method that includes a step of contacting a urine sample with an antibody for a renal tubular cell injury biomarker, which is not a limitation of Group IV; (b) the invention of Group II includes a step of providing a treatment to a subject which is not a limitation of Group IV; and (c) the invention of Group IV includes a step of determining the extent of injury relative to the time of an event, which is not a limitation of Groups I or II.

In regards to (a), the antibody detection step is a specific example of the method of detecting NGAL in urine, which is a limitation of all the claims. In regards to (b) and (c), as discussed in paragraph 0042, the "method of the invention can be used to detect the onset of renal tubular cell injury, and to monitor the treatment thereof, for a wide variety of events" which include "administration of pharmaceuticals, ... or other medicament substances to a subject" such as nephrotoxins and both "newly-developed and well-known compounds". In other words, the "event" of Group IV may encompass the "treatment" of Group II, and vice versa.

In addition to the foregoing allegations, Applicants respectfully disagree with the Examiner's position in Section 5 that the inventions of Groups I, II and IV are distinct as having acquired a separate status in the art, or that searches required for one group are not required for the other. First, all these methods of Groups I, II and IV relate to subjects who are suspected of having or being prone to develop a renal tubular cell injury. Second, all these method Groups relate to identifying the presence of a biomarker for renal tubular cell injury (NGAL) in the subject's urine. Third, Applicants contend that each of Claims 1, 30, 46, 6 and 24 would appear to be capable of being used together, as lacking a materially different "design, mode of operation, function or effect", and as such that they "overlap in scope; i.e. they are not mutually exclusive". On this basis, applicants submit that it would not constitute a serious burden for the Examiner to search and examine the inventions of Groups I, II, and IV at the same time.

In regards to the species election requirement set forth in Section 6, in the event the Examiner reconsiders and withdraws restriction of Group IV but yet maintains the species election, Applicants elect Event i., surgical procedures (Claims 26-27). It is believed, however, that claims 26 and 27 as currently amended are not subject to species election.

## CONCLUSION

Applicants believe a full and complete response to the Action has been made.

Respectfully submitted,

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By _____

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